Stimulus Novelty Differentially Affects Attentional Allocation in PTSD

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Background: *This study investigated attentional allocation in 39 Vietnam combat veterans, 25 with and 14 without posttraumatic stress disorder, assessing P300 amplitudes and latencies during both three-tone and novelty "oddball" tasks.*

Methods: *The three-tone oddball task consisted of three stimuli: frequent tones (85%), rare target tones (7.5%), and rare distractor tones (7.5%). The novelty oddball task was identical to the three-tone task except that the rare distractor tones were replaced with nonrepeating novel sounds (7.5%).*

Results: *Combat veterans with posttraumatic stress disorder showed significant P300 amplitude enhancements at frontal sites in response to distracting stimuli during the novelty but not during the three-tone oddball tasks. There were no amplitude differences in target tones during either task.*

Conclusions: *The data suggest that combat veterans with posttraumatic stress disorder demonstrate P300 responses consistent with a heightened orientation response to novel, distracting stimuli. This finding is consistent both with the clinical presentation of the disorder and with theoretical notions that individuals with posttraumatic stress disorder demonstrate information-processing biases towards vague or potentially threatening stimuli.* Biol Psychiatry 2000; 47:880–890 © *2000 Society of Biological Psychiatry*

Key Words: PTSD, attention, P300, novelty, ERP, orienting

Introduction

Difficulties with attention are some of the most common complaints among individuals diagnosed with posttraumatic stress disorder (PTSD). The scope of these complaints is quite broad, encompassing both increased attention to potentially threatening cues in the environment and difficulty sustaining attention on target tasks. These two patterns of attentional difficulties have been roughly captured in the DSM-IV (American Psychiatric Association 1994) as "hypervigilance" and "difficulty concentrating," respectively. Although it is apparent that abnormalities in attention exist in PTSD, the circumstances in which attentional functioning in PTSD is either intact or deficient have only begun to be investigated.

Event-related potential (ERP) studies provide an opportunity to better understand attentional processing in PTSD. In particular, the P300 component of the ERP has been shown to be particularly sensitive to attentional allocation. In nondisordered samples, the P300 is maximal at frontal sites (often called the P3a) when the subject is exposed to loud, novel, or salient stimuli, whereas the P300 is maximal at parietal sites (often called the P3b) when the subject is instructed to attend to stimuli (Johnson 1986; Snyder and Hillyard 1976). Whereas the P300 in general is thought to represent "context updating" (Donchin and Coles 1988), investigators have separately interpreted the P3a as a reflection of passive attentional switching or "orienting," and the P3b as an index of an executive ability to sustain attention to a target stimuli (Naatenen 1990). The sensitivity of the P300 to attentional allocation makes this component particularly relevant in the investigation of sustained attention difficulties and attentional biases associated with PTSD.

In general, differences in the amplitude, habituation, and typical frontal/parietal topography of the P300 have been associated with various structural, neurochemical, and cognitive abnormalities. Damage to both the hippocampus and the temporal–parietal junction has been associated specifically with frontal P300 (P3a) amplitude reductions in stroke patients (Knight 1984; Knight et al 1989). P300 amplitude and latency also vary as a function of psychopharmacologic administration (lorazepam: Pooviboonsuk et al 1996; amitriptyline: Rimpel et al 1995) and neurotransmitter levels (serotoninergic: Hansenne et al 1998; cholinergic: Dierks et al 1994). In relation to cognitive functioning, Fabiani et al (1998) found that frontally shifted P300s to target tones (stimuli that typically have a parietal vertex) are associated with poor performance in neuropsychologic tests of frontal lobe

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functioning in elderly subjects. Friedman et al (1998) found that elderly subjects did not show habituation in frontal P300 to novel sounds, as did younger subjects, and suggested the absence of habituation also reflected poor frontal lobe functioning. Thus, in addition to illuminating aspects of attentional performance, P300 investigations in PTSD may point to associated structural, neurochemical, or cognitive abnormalities.

Most studies investigating the P300 response in PTSD have used the three-tone "oddball" task. In this task, subjects are asked to count silently or press a button to hear rare target tones interspersed among a series of frequent tones and rare distractor tones. Rare target tones are distinguished from rare distractor tones by stimulus frequency (i.e., pitch) and by the task demands. Whereas the subject is asked to attend to the rare target tones, they typically are asked to ignore the rare distractor tones. McFarlane et al (1993) studied firefighters with PTSD using a three-tone oddball task. They found reductions in the P300 component in response to both rare target tones and rare distractor tones and interpreted this pattern as indicative of a generalized attentional deficit in PTSD. The McFarlane et al (1993) findings were supported by a two-tone oddball study (Charles et al 1995) in which P300 reductions to target tones were found in nonmedicated crime victims with PTSD. Metzger et al (1997) also found P300 reductions to target tones in a three-tone oddball task in nonmedicated PTSD subjects, but not in medicated ones.

Lately, initial speculations concerning a general attentional deficit in PTSD have been challenged. This challenge stems from other ERP studies showing enhanced P3a amplitudes in response to trauma-relevant or novel stimuli, at least when those stimuli serve as distractors in an ongoing oddball task (Bleich et al 1996; Kimble et al 1997; Neylan et al 1996). Kimble et al (1997) and Neylan et al (1996) utilized novelty oddball paradigms in which nonrepeating, ambiguous, rare distractor sounds were placed among a series of frequent tones and equally rare target tones. Both studies reported increased frontal P300s (P3a) in response to the novel distractors and normal P300 responses in response to target tones (P3b). Using an independent sample, Neylan et al (1998) did not replicate P3a enhancements in PTSD unless group differences in age and education were covaried out (T. Neylan, personal communication, December 1998). Bleich et al (1996) modified the auditory novelty task in a P300 study of Israeli combat veterans. In this task, rare combat picture distractors (19%) were randomly placed among a series of both frequent neutral pictures (62%) and rare, affectively neutral target pictures (19%). This design resulted in P300 enhancements to combat picture distractors in veterans with PTSD, with no P300 reductions to target stimuli. In another modified visual oddball task, Kounios et al (1997) presented rare target food words (16%) among a series of frequent neutral words (42%) and frequent trauma words (42%). They reported enhancements in a 250–350-msec time window to both types of frequent words, including the trauma words, in PTSD subjects, whereas combat comparison subjects showed a distinct negativity. These studies seem to indicate subjects with PTSD may demonstrate biases in attentional allocation toward novel or trauma-relevant material incidental to an ongoing task.

The fact that some P300 studies show enhancements to distractors and others do not poses the possibility that the novelty of the distracting stimulus differentially affects attentional allocation in PTSD. Findings across studies suggest PTSD subjects may show heightened attention to distracting stimuli that are trauma-relevant or novel (Bleich et al 1996; Kimble et al 1997; Neylan et al 1996) but not to distractors that are repeating (McFarlane et al 1993; Metzger et al 1997). However, this hypothesis has not been tested empirically.

The discrepancy in the P300 findings regarding target stimuli raises the additional possibility that attention to target tasks in PTSD is differentially affected by the context in which the processing occurs. This question arises from differences in findings between three-tone oddball studies in which reductions in P3b are typically found in response to target stimuli (Charles et al 1995; McFarlane et al 1993; Metzger et al 1997) and the novelty oddball studies where normal P3bs have been demonstrated (Bleich et al 1996; Kimble et al 1997; Neylan et al 1996). Consequently, it appears that PTSD is characterized by P300 deficits in response to target tones when the distracting stimuli are repeated tones, and an intact P300 in response to target stimuli when the distracting stimuli are novel and nonrepeating.

Our study was designed to investigate two questions related to stimulus processing by individuals with PTSD: 1) whether the novelty of the distracting stimuli differentially affects attentional allocation to those stimuli in PTSD and 2) whether the attention allocated to target stimuli is affected by the context in which that processing occurs. Combat veterans with and without PTSD were administered both three-tone and novelty oddball tasks. It was predicted that veterans with PTSD would show enhancements in the P300 in response to ambiguous, nonrepeating distractor sounds. We also predicted reduced P3s in response to target tones for PTSD veterans during the three-tone oddball task and no such reductions during the novelty oddball task (replicating previous findings).

Methods and Materials

Forty-one right-handed male combat veterans participated in the study; 24 were diagnosed with PTSD, 15 without PTSD, and two

subjects were dropped from the study due to incomplete diagnostic information. Participants were recruited from a database containing eligible volunteers from previous studies at the Behavioral Science Division of the National Center for PTSD. Potential participants were contacted by phone and screened to exclude those with a history of epilepsy or seizures and/or neurologic or medical disorders that might compromise neurologic functioning. An absence of exposure to combat during military service and a diagnosis of substance abuse or dependence within the past year were also conditions for exclusion. All veterans served in the Vietnam era and were exposed to at least "light" combat according to the Combat Exposure Scale (CES; Keane et al 1989).

All subjects participated in two experimental sessions. The first session began with a written informed-consent procedure. This was followed by administration of the Anxiety, Mood, Psychosis, and Substance Abuse modules of the Structured Clinical Interview for the DSM-III-R, patient version (Spitzer et al 1990), the Clinician Administered PTSD Scale (CAPS; Blake et al 1995), the Beck Anxiety Inventory (BAI; Beck and Steer 1990), the Beck Depression Inventory (BDI; Beck and Steer 1987), and the CES. All interviews were conducted by trained clinical psychologists or clinical psychology graduate students.

The second session consisted of a series of ERP tasks. Participants sat in a comfortable chair approximately 1.5 m from a 21-in color monitor on which a fixation point was presented. Event-related potentials were measured from 64 tin-plate electrodes embedded in an elastic cap (Electro-cap International, Eaton, OH) and referenced to an electrode affixed to the left mastoid. Cz, fp1, and fp2 electrodes were placed using an augmented 10-20 System electrode placement with all other electrodes positioned automatically at standard relative distances (American Electroencephalographic Society 1991). A vertical electro-oculogram was recorded using a right supraorbital electrode, and the horizontal electro-oculogram was recorded from an electrode placed on the left canthus. Electrode impedances were maintained below 5000 Ω (5 kΩ) at all reference and recording electrodes. Each subject's electroencephalogram (EEG) was amplified 50,000 times using an SA Instrumentation (San Diego) DC amplifier, sampled at the rate of 256 Hz, with a high-pass filter at 0.01 Hz and the low-pass filter at 100 Hz. Recording commenced 100 msec before stimulus onset and continued for 1 sec. Event-related potential epochs were stored offline on a Digital Equipment Corporation 486 personal computer for later analyses. All data acquisition, filtering, and averaging were completed using InstEP Systems (Ottowa) software.

Tasks

Once the electrodes were secure, the subject was instructed about the task. All subjects engaged in two ERP tasks. The first was a three-tone oddball task that consisted of binaural presentations of 600 auditory stimuli through earphones. Presentations occurred in blocks of 200 stimuli, 85% of which were 1000-Hz, 80-dB pure tones ("frequents") presented for 50 msec with a rise-and-fall time of 5 msec; 7.5% of which were rare 2000-Hz "target" tones that were identical in all other parameters to the frequent tones; and 7.5% of which were rare, pure-tone "distractors" of 500 Hz. The interstimulus interval was 1100 msec. For the entire task, 510 frequent stimuli, 45 distracting stimuli, and 45 target stimuli were presented.

The novelty oddball task was identical to the three-tone oddball task except that the distractor tones were replaced with nonrepeating, digitized novel sounds of 200 msec in duration. These novel sounds were primarily computer-generated whistles and buzzes as well as unidentifiable sounds (clunks, pings, buzzes, etc.) taken from a sound effects compact disk. The intensities of all stimuli including novel sounds were checked using a calibrated sound-level meter (Radio Shack 33-2055) and adjusted so the perceived intensity by the subject was 80 dB.

For the three-tone oddball task, the subject was told he would be hearing a series of tones in which target high-pitched tones were randomly interspersed. He was asked to ignore all other tones, and to push a button as quickly and as accurately as possible when a high-pitched target tone was heard. For the novelty P300 task, the subject was instructed he would be hearing rare, high-pitched target tones presented among a series of frequent tones and rare, novel sounds. He was asked to ignore all other stimuli but the target tones. When a target tone was presented, the subject was asked to press a button with his dominant hand. When the subject indicated he understood the instructions, two Etymotic Research (Elk Grove Village, IL) ER-3 ABR Tubephone earphones were placed in his ears.

All EEG epochs and reaction times were stored offline for later analyses. Trials contaminated with blink artifact were removed manually. For each subject, all artifact-free trials were averaged per condition (frequent, target, distractor) and filtered with a low-pass digital filter of 15 Hz. The P300 was measured using a baseline-to-peak measure and was specified as the most positive data point between 250 and 600 msec.

Results

The goals of the analysis were threefold: 1) to summarize demographic characteristics of the sample and test for potential group differences in age, education, and combat exposure; 2) to analyze accuracy and reaction time in the button-pressing response to target stimuli; and 3) to investigate possible group differences in the processing of target tones and distracting stimuli during both the novelty and the three-tone oddball tasks.

Demographic variables were analyzed (Goal 1) using planned *t* tests between variables of interest. Hits, false alarms, and reaction time were analyzed (Goal 2) using separate 2 × 2 analyses of variance (ANOVAs) with Group (PTSD vs. No PTSD) as the between-subjects variable and Task (Three-Tone vs. Novelty) as the within-subjects factor. Group effects (Goal 3) were analyzed using a 2 × 2 × 2 × 3 × 3 repeated-measures ANOVA that used Group (PTSD vs. No PTSD) as the between-subjects factor and Task (Novelty vs. Three-Tone), Stimulus (Distractor vs. Target), Topography (Frontal, Central, Parietal), and Electrode (Central, Left, Right) as the

Table 1. Age, Education, Combat Exposure, and Symptom Reports

	PTSD (n = 24)		No PTSD (n = 15)			
	Mean	(SD)	Mean	(SD)	t	p
Age (years)	49.8	(3.8)	50.1	(4.4)	−0.22	>.1
Education level (years)	14.3	(2.3)	14.9	(3.1)	−0.65	>.1
Combat Exposure Scale score	26.0	(9.6)	17.8	(12.0)	2.23	<.05
Total CAPS score	70.7	(23.5)	7.4	(10.3)	11.50	<.001
CAPS B score	19.8	(8.1)	0.17	(1.9)	11.16	<.001
CAPS C score	26.9	(12.4)	3.1	(6.5)	7.89	<.001
CAPS D score	23.9	(6.5)	3.7	(4.5)	11.50	<.001
Beck Anxiety Inventory score	23.3	(16.5)	1.8	(2.0)	6.32	<.001
Beck Depression Inventory score	25.9	(12.8)	4.5	(3.9)	7.65	<.001

PTSD, posttraumatic stress disorder; CAPS, Clinician Administered PTSD Scale.

within-subjects factors. Topography was used as a within-subjects factor in these analyses, given that P300 responses of different topographies likely represent distinct cognitive phenomena (Katayama and Polich 1998). The Electrode factor consisted of three montages (Central, Left, Right), each consisting of three electrodes (Central: Fz, Cz, Pz; Left: F1, C1, P1; Right: F2, C2, Pz). The Left and Right levels of the Electrode factor were electrodes placed immediately adjacent to the central sites as per guidelines published by the American Electroencephalographic Society (1991) and thus do not represent laterality effects. Therefore, the analyses emphasized a midline, sagittal chain of electrodes that could discriminate frontal, central, and parietal effects while assuring the entire analyses were not based on effects from only three electrodes (Fz, Cz, Pz). All reported degrees of freedom and subsequent p values are based on adjustments made using the Geisser-Greenhouse correction to account for violations in sphericity in the repeated-measures design. Follow-up analyses of covariance were conducted to assess the possible effects of group differences on combat exposure. Additional follow-up analyses were completed with and without subjects manifesting comorbid panic disorder to assure that PTSD-related group differences were not attributable to this subgroup (Clark et al 1996; Metzger et al 1997). All analyses were carried out using SPSS (Chicago) Version 8.0.

Subject Demographics

Twenty-four combat veterans were diagnosed with current PTSD (PTSD). They were compared with 15 combat veterans never diagnosed with PTSD (No PTSD). Subject demographics are summarized in Tables 1 and 2. The groups did not differ on age and years of education. Although all subjects were exposed to at least light combat according to the CES (Keane et al 1989), PTSD veterans reported significantly higher exposure to combat than did the No PTSD group. As expected, PTSD veterans also scored higher on the BAI, the BDI, and clusters B, C, and D of the CAPS.

Group Effects

BEHAVIORAL RESULTS. Groups did not statistically differ in reaction time, hits, or misses in response to target stimuli. Accordingly, false alarms did not differ with regard to either frequent tones or distracting stimuli during either task.

P300 AMPLITUDE. The planned ANOVA revealed a single, significant four-way Group × Task × Stimulus ×

Table 2. Race, Service Branch, Medication, and Comorbid Diagnoses

	PTSD (n = 24)	No PTSD (n = 15)	Total (n = 39)
Race			
White	19	14	33
African American	5	1	6
Service branch			
Army	12	9	21
Navy	4	1	5
Air Force	4	1	5
Marines	4	4	8
Medications			
Serotonin reuptake inhibitors	6	0	6
Atypical antidepressants	5	0	5
Tricyclic antidepressants	1	0	1
Mood stabilizers	1	0	1
Anxiolytics	1	0	1
Anticonvulsants	1	0	1
Comorbid diagnoses			
Bipolar I	1	0	1
Major depression	6	0	6
Dysthymia	3	0	3
Panic disorder	3	0	3
Obsessive-compulsive disorder	3	0	3
Generalized anxiety disorder	2	0	2
Simple phobia	2	2	4

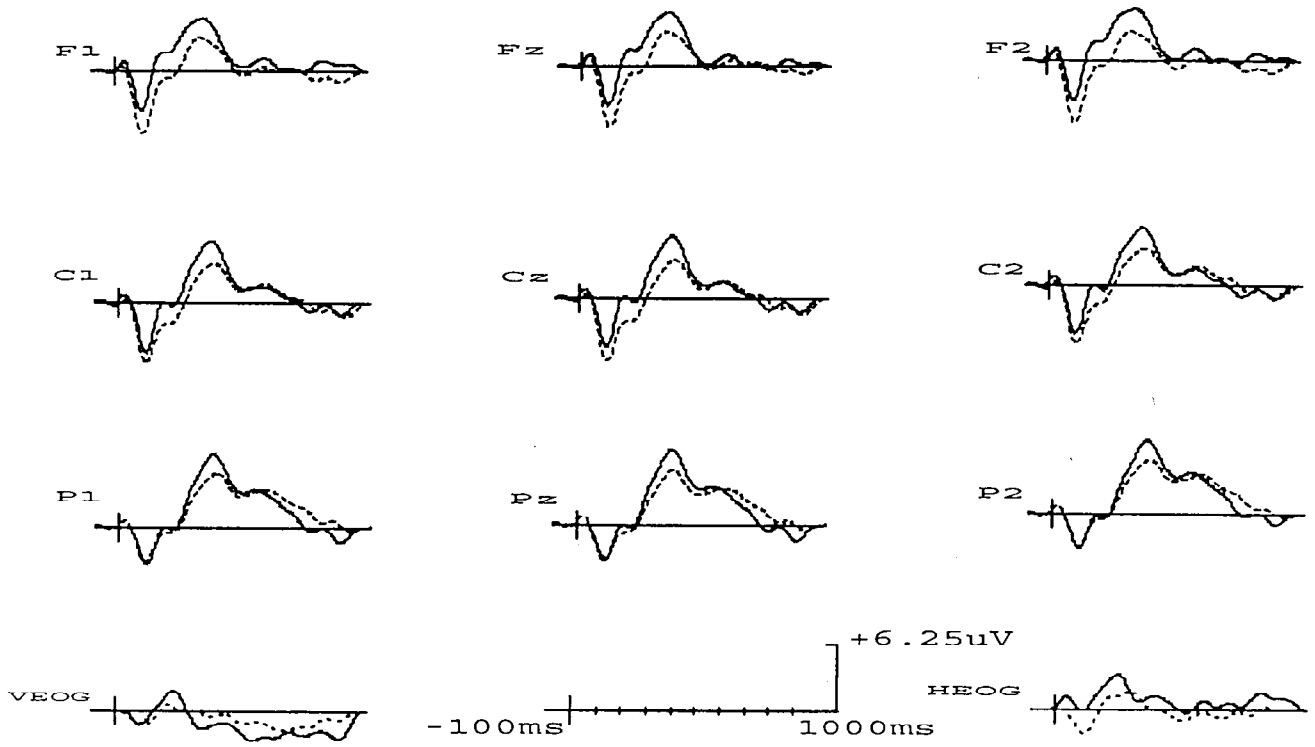

Figure 1. Event-related potentials in response to repeating distractor tones during the three-tone task in Posttraumatic Stress Disorder (PTSD; dashed lines) and No PTSD (solid lines) subjects. ms, msec.

Topography interaction [$F(1.4,74) = 5.2$, $p = .02$] for P300 amplitude. There was no main effect for Group nor were there any additional interactions with the Group factor. The four-way interaction remained significant when controlling for differences between the groups on combat exposure [$F(1.4,72) = 4.3$, $p = .03$], and when subjects with panic disorder ($N = 3$) were removed from the PTSD sample [$F(1.4,66) = 5.3$, $p = .02$]. Post hoc analysis revealed the four-way interaction was due to differences between groups at frontal sites in the processing of distracting sounds. The three-way ANOVA (Group × Task × Topography) was significant for distracting stimuli [see Figures 1 and 2; $F(1.5,74) = 3.5$, $p = .05$] but not for target stimuli [see Figures 3 and 4; $F(1.4,74) = 1.4$, $p = .51$]. Further analyzing the significant effect to distracting stimuli resulted in a single Group × Task interaction that was present at frontal sites [$F(1,37) = 4.3$, $p = .05$] but not at central [$F(1,37) = 0.06$, $p = .81$] or parietal sites [$F(1,37) = 0.02$, $p = .89$]. At the follow-up comparisons for the significant interaction at the frontal sites using t tests, no statistically significant differences for novel sounds [$t(37) = 1.02$, $p = .32$] or distracting tones [$t(37) = -0.98$, $p = .33$] were found between the two groups. This pattern of findings indicates that PTSD subjects showed P300 enhancements in response to distracting stimuli during the novelty task (novel sounds), but only relative to P300 reductions in response to distracting stimuli during the three-tone task (repeated distracting tones).

Group differences in the processing of novel sounds do not appear to be due to a differential rate of habituation to these novel sounds across the three blocks. Although both groups showed means consistent with decreased amplitudes in Block 3 as compared with Block 1, this was not significant and there was no differential pattern between groups. Using a 2 × 2 × 3 mixed-model ANOVA in which Group was the between-subjects factor and Block (Block 1, Block 3) and Electrode (fz, cz, pz) were the within-subjects variables, there was no main effect for Block [$F(1,,27) = 0.16$, $p = .69$] nor were there any interactions with Group. The lack of statistically significant habituation is not surprising given the age of the subjects, the averaging of 15 stimuli per block, the uniqueness of the novel sounds, and the infrequency with which the novel stimuli were presented (7.5% of the trials).

Task, Stimulus, Topography, and Electrode Effects

The five-way ANOVA also revealed significant within-subject main effects and interactions. There were significant main effects for Stimulus [$F(1,37) = 9.1$, $p = .00$], Topography [$F(1.3,74) = 9.6$, $p = .001$], and Electrode

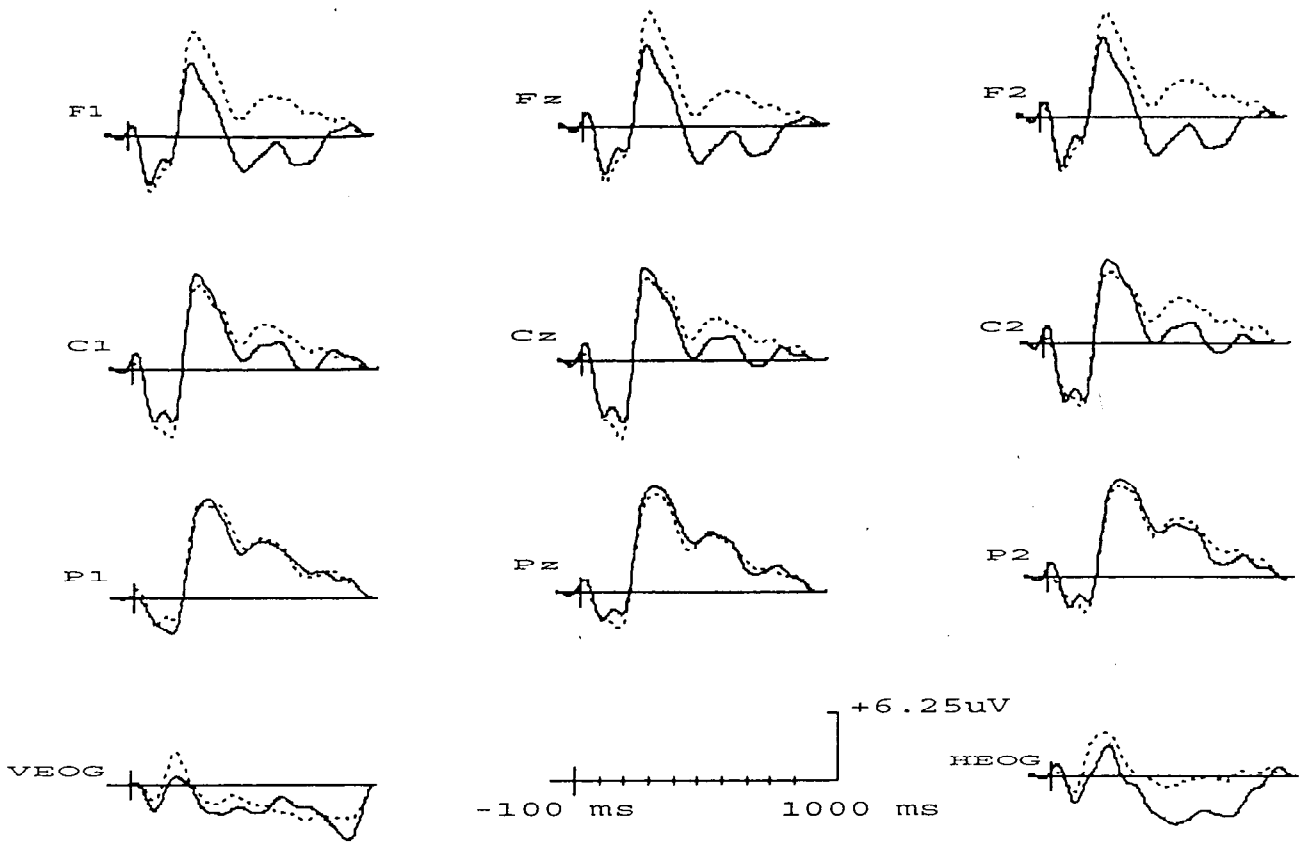

Figure 2. Event-related potentials in response to nonrepeating novel sounds during the novelty task in Posttraumatic Stress Disorder (PTSD; dashed lines) and No PTSD (solid lines) groups. ms, msec.

[$F(1.8,74) = 5.3, p = .01$], which represent, across tasks, larger overall amplitudes in response to distractor tones (Stimulus), larger parietal amplitude (Topography), and larger sagittal amplitudes (Electrode). There was also a significant Task × Stimulus interaction [$F(1,37) = 25.3$, $p = .00$]. During the novelty task, both groups showed P300 enhancements in response to distractors (novel sounds) and P300 reductions in response to targets as compared with comparable stimuli in the three-tone task, a finding that has been reported previously in noncombat samples (Grillon et al 1990). An expected Stimulus × Topography interaction was also present across groups with a parietally shifted P300 present in response to rare stimuli regardless of task and a more frontally shifted P300 in response to distracting stimuli regardless of task [$F(1.6,74) = 5.7, p = .01$; see Figures 5 and 6]. No other significant interactions were present in the data.

Discussion

In our study combat veterans with PTSD demonstrated a pattern of electrophysiologic responses consistent with alterations in attention to distracting stimuli. At frontal electrode sites, PTSD subjects, as compared with combat controls, had larger P300s in response to novel sounds but smaller P300s in response to rare, repeated distracting tones. This PTSD-related attentional bias occurred in the absence of any statistically significant differences in P300 amplitude in response to target or task-relevant stimuli. The evidence for P300 enhancements in response to novel stimuli in this study is consistent with other studies demonstrating larger P300s in PTSD in response to novel and/or trauma-relevant stimuli when they serve as distractors in an ongoing task (Bleich et al 1996; Neylan et al 1996).

Lately there has been a considerable effort to define whether repeated distracting stimuli, like those presented in the three-tone oddball task, elicit a P3a response or a P3b response (Katayama and Polich 1998). Such differentiation has interpretive significance, as the P3a and P3b are thought to represent unique cognitive processes (Falkenstein et al 1993) and are likely to have different anatomic generators (Knight 1984, 1996). There has been increasing evidence of late to suggest that the rare, repeated distractor tones produce a parietal P3b response (Katayama and Polich 1998). Thus, the ERP stimuli in these tasks that typically produce the P3b response (the target tones and the repeating distractors) are consistently smaller in mean

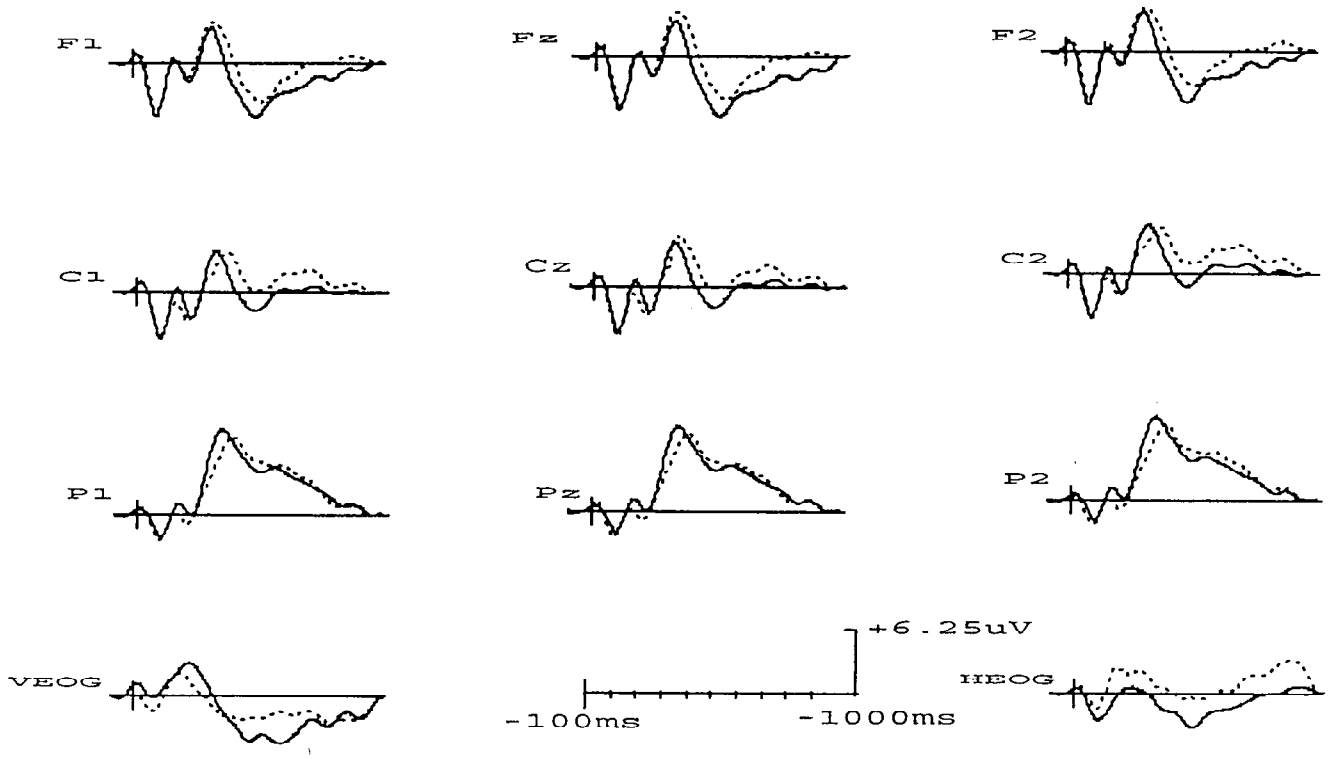

Figure 3. Event-related potentials in response to target tones during the three-tone task in Posttraumatic Stress Disorder (PTSD; dashed lines) and No PTSD (solid lines) subjects. ms, msec.

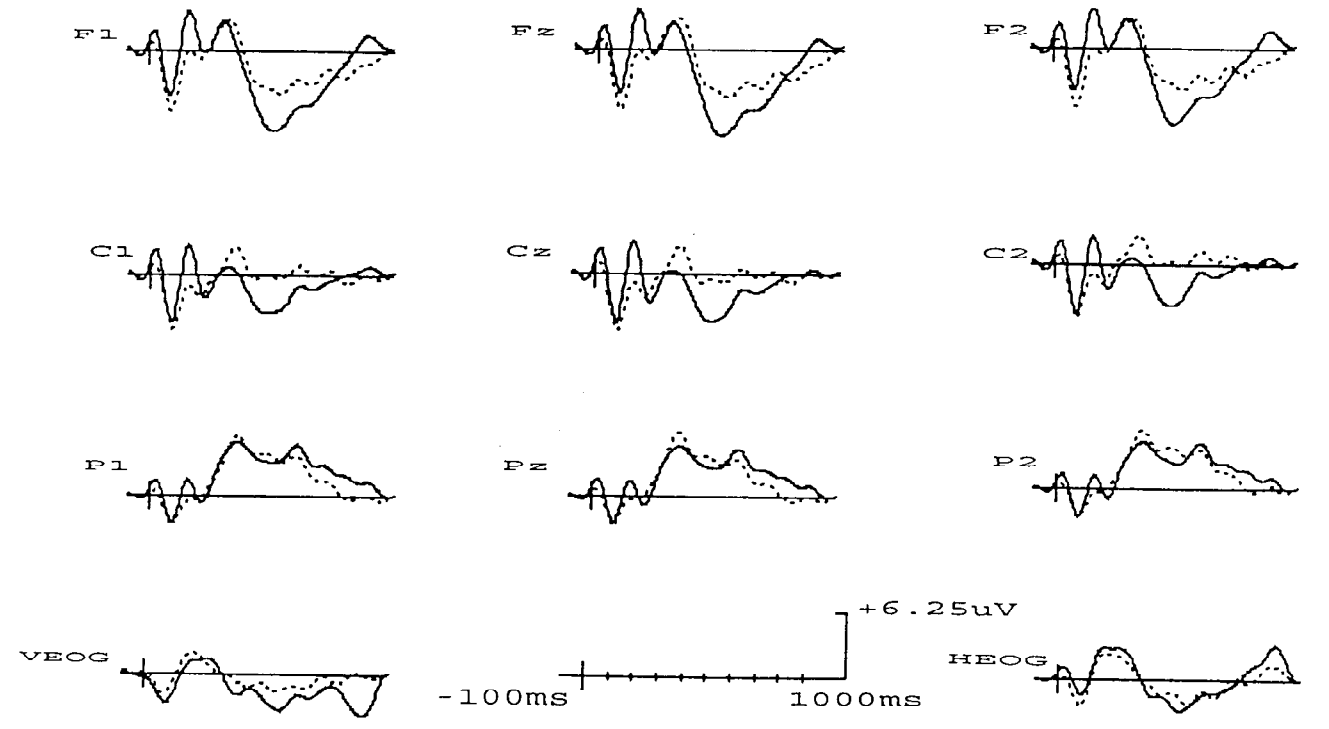

Figure 4. Event-related potentials in response to target tones during the novelty task in Posttraumatic Stress Disorder (PTSD; dashed lines) and No PTSD (solid lines) subjects. ms, msec.

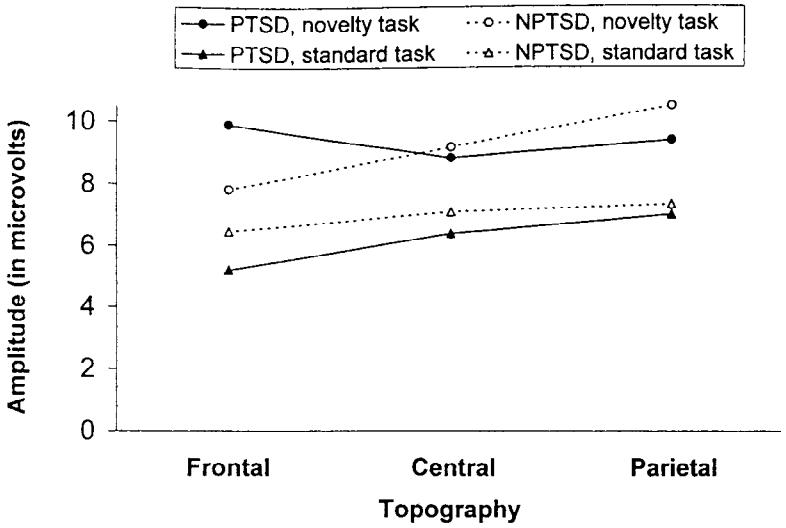

Figure 5. Posttraumatic Stress Disorder (PTSD) and No PTSD P300 amplitudes across frontal, central, and parietal sites in response to distracting stimuli. Posttraumatic Stress Disorder subjects show smaller P300 amplitude in response to both types of distracting stimuli at central and parietal electrodes. At frontal sites, however, PTSD subjects demonstrate larger P300s in response to the novel distracting sounds but smaller P300s in response to the repeating distractor tones.

amplitude in PTSD subjects. Accordingly, the novel stimulus, which is known to reliably produce the P3a response, produces larger P3a amplitudes in the PTSD subjects. The overall pattern in PTSD is one of reduced P3bs and enhanced P3as, a pattern that achieves statistical significance at frontal sites where P3a is maximal.

Therefore, the frontal PTSD-related P3a enhancements to novel sounds are an interaction, and thus significant only in relation to the frontal PTSD-related P3b decrements to repeated, distracting tones (see Figure 5). For the most part, PTSD subjects showed smaller mean amplitudes in response to all distracting stimuli, at all topographies, and during both tasks. The sole statistically significant exception is the P3a enhancement to novel stimuli at frontal sites. It is the specificity of this statistically significant P300 enhancement, as well as the well-defined characteristics of the P3a, that supports our conclusions of a heightened orienting response to novel stimuli in PTSD. In general, however, PTSD subjects showed a smaller mean amplitude P300 in response to all distracting stimuli at all sites—a finding where one could alternatively argue for a lack of attention to distracting stimuli in the disorder.

This pattern of findings is intriguing, as it fits with the theoretical nature of PTSD as a disorder founded on heightened apprehension and sensitivity to threat as well as the clinical presentation of concentration problems on task-related activities and hypervigilance to distracting, unusual, and, perhaps, trauma-relevant stimuli (Litz and Keane 1989).

The design of the study did not control for potential order effects, as all subjects performed the three-tone task prior to the novelty task. However, analysis of the data

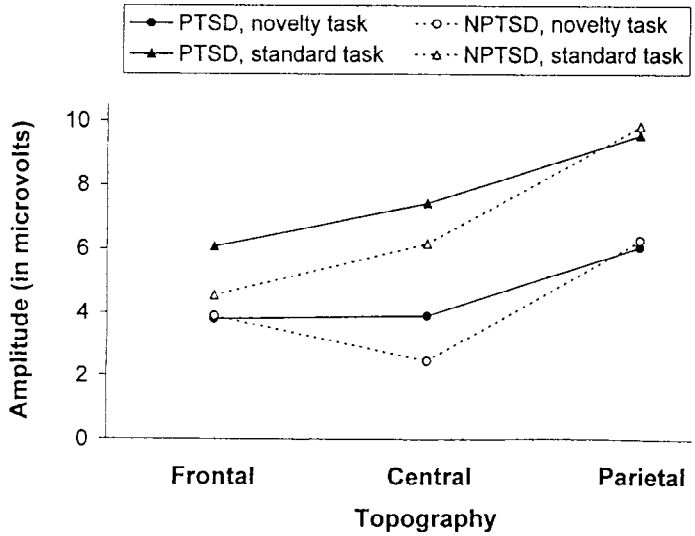

Figure 6. Posttraumatic Stress Disorder (PTSD) and No PTSD P300 amplitudes across frontal, central, and parietal sites in response to target stimuli. While both groups showed reductions in P300 amplitude during the novelty as compared with the standard three-tone task, the prediction that PTSD subjects would show significantly larger P300 reductions in response to target tones during the novelty task was not supported.

suggest that "Order" was not a confound in this study. Although both groups showed amplitude decreases in the P300 in response to novel sounds across block presentations, neither group showed differential habituation. The fact that individuals with PTSD showed enhanced P300 during the second novelty task (Blocks 4, 5, and 6, overall), when typically one would expect decrements associated with habituation, further suggests it was the novel stimuli and not the order of presentation that is the basis for the larger PTSD-related frontal P3as.

There were no overall group differences in the parietal P3b component in response to target tones. This finding contradicts at least three studies of similar sample sizes that have found reductions in P300 in response to target tones using auditory oddball tasks (Charles et al 1995; McFarlane et al 1993; Metzger et al 1997). However, those studies differ from our study in a number of significant ways. McFarlane et al (1993), for example, used a nontraumatized, mixed, civilian control group; Charles et al (1995) used an unmedicated, acutely traumatized PTSD group; and Metzger et al (1997) found P3 reductions in their unmedicated sample only. These methodological and sampling differences could account for differences in the findings, and our study suggests there are at least subgroups of PTSD subjects in which P3b is likely to be intact. This discrepancy in the findings weakens what was a growing consensus regarding P3b reductions in individuals with PTSD (Pitman 1997; Pynoos et al 1997). Instead, the findings across studies suggest a complicated picture in which P3b amplitude and sustained attention could be affected by factors such as medication and comorbid diagnosis (Metzger et al 1997), the chronicity of the disorder (Charles et al 1995), and trauma exposure (McFarlane et al 1993).

In addition, the presence of novel, distracting stimuli during the oddball tasks did not differentially affect P300 amplitude in response to target stimuli in PTSD subjects. Rather, both groups showed P300 decrements in response to target tones during the novelty task (as compared with the three-tone task) as evidenced by a robust Task × Stimuli interaction. Decreases in P300 amplitude in response to target stimuli during the novelty task have been reported previously in the literature and are thought to represent shifts in attention away from target stimuli toward the novel stimuli (Katayama and Polich 1998). However, these shifts were not group specific in this study, and thus the findings do not indicate that the ability to sustain attention on relevant tasks in PTSD is influenced by the nature of the distracting stimuli in the environment.

This study, in combination with previous work, highlights a number of important issues regarding P300 work in PTSD. The fact that subjects with PTSD appear to show P300 enhancements in response to novel and trauma-relevant stimuli, but only when they serve as distractors in an ongoing task, illuminates the potential interaction between stimulus content (generally threatening, novel, trauma relevant) and task demands (distractor vs. target) when assessing attention using the P300. When novel and/or trauma-relevant stimuli are used as target stimuli during a task (Kimble et al 1997; Metzger et al 1997), the task requirements to attend to the stimulus may account for the majority of variance in the amplitude of the P300 response, and thus PTSD-related enhancements are not found. Whereas subjects with PTSD may also be showing enhancements in the P300 in response to novel/trauma-relevant stimuli when they serve as targets, this group-specific effect may be masked by the task demands that create enhancements in the P300 in both groups. Therefore, fruitful research in PTSD might systematically examine the interaction between stimulus content (i.e., novelty, trauma relevance, generally threatening) and task demands (i.e., distractor or target).

Additionally, the field faces the further challenge of demonstrating possible differences between generally novel and specifically trauma-relevant stimuli. Evidence from outside the field of electrophysiology suggests individuals with PTSD may be biased in their stimulus processing of a range of threatening, startling, or novel stimuli regardless of their trauma relevance. Both cognitive reaction–time studies (Litz et al 1996) and startle paradigms (Morgan et al 1995) have suggested PTSD may be characterized by an overgeneralized response to a wide range of unusual or threatening stimuli. In addition, future studies would also be improved through the inclusion of a nontrauma control group to aid in sorting out the effects of traumatic experiences from the effects of PTSD on attentional allocation. Ultimately, defining the stimuli to which individuals with PTSD preferentially allocate attention would improve our understanding of both the cognitive and the pathophysiologic characteristics of the disorder.

Summary

Posttraumatic stress disorder has been characterized both theoretically and clinically as a disorder that manifests attentional biases towards novel or trauma-relevant stimuli in the environment. This study has produced specific electrophysiologic evidence consistent with a selective sensitivity to novel, distracting sounds. This finding suggests that clinical phenomena such as hypervigilance may have neurophysiologic correlates that may be valuable in identifying both the structural and the pharmacologic basis for this behavior. The specificity of the frontal enhancements in response to novel sounds, in the presence of

decrements in response to all other stimuli, suggests that the P3a component and its biological correlates warrant further investigation and may lead to an improved understanding of the pathophysiology of the disorder.

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